In th Claims

1. (Original) A method of inhibiting angiogenesis comprising:

(a) identifying a patient in need of an angiogenesis inhibitor; and

(b) administering to the patient a therapeutically effective amount of a PPAR gamma ligand, wherein angiogenesis is inhibited in the patient.

2. (Original) The method of claim 1, wherein the patient is a mammal.

3. (Original) The method of claim 2, wherein the mammal is human.

4. (Original) The method of claim 1, wherein the therapeutically effective amount of a PPAR gamma ligand is an angiogenesis inhibiting amount.

5. (Original) The method of claim 1, further comprising administering a therapeutically effective amount of an RXR receptor ligand.

6. (Original) The method of claim 1, wherein the PPAR gamma ligand is selected from the group consisting of (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy] phenyl]methyl]-2,4-thiazolidinedione: (troglitazone); 5-[4-[2-(5-ethylpyridin-2-yl) ethoxyl]benzyl]thiadiazolidine-2,4-dione:(pioglitazone); 5-[4-[(1-methylcyclohexyl) methoxy]benzyl]thiadiazolidine-2,4-dione: (ciglitazone); 4-(2-naphthylmethyl)- 1,2,3,5- oxathiadiazole-2-oxide; 5-[4-[2-[N-(benzoxazol-2-yl)-N-methylamino]ethoxy]benzyl]-5-methylthiazolidine-2,4-dione; 5-[4-[2-[2,4-dioxo-5-phenylthiazolidin-3-yl) ethoxy] benzyl]thiazolidine-2,4-dione; 5-[4-[2-[N-methyl-N-(phenoxycarbonyl)amino] ethoxy] benzyl]thiazolidine-2,4-dione; 5-[4-[2-phenoxyethoxy) benzyl]thiazolidine-2,4-dione; 5-[4-[2-(4-chlorophenyl) ethylsulfonyl] benzyl]thiazolidine-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl) propionyl]benzyl]thiazolidine-2,4-dione; 5-[[4-(3-hydroxy-1-methylcyclohexyl) methoxy]benzyl]thiadiazolidine-2,4-dione; 5-[4-[2-(5-methyl-2-phenyloxazol-4-yl) ethoxyl]benzyl]thiadiazolidione-2,4-dione; 5-[(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl]thiadiazoline-2,4-dione: (englitazone); 5-[[2-(2-naphthylmethyl) benzoxazol]-5-ylmethyl] thiadiazoline -2,4-dione; 5-[4-[2-(3-phenylureido)ethoxyl] benzyl]thiadiazoline-2,4-dion ; 5-[4-[2- [N-(benzoxazol-2-yl)-N-

methylamino] ethoxy]benzyl]thiadiazoline-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl) propionyl] benzyl]thiadiazoline-2,4-dione; 5-[2-(5-methyl-2-phenyloxazol-4-ylm thyl) benzofuran- 5-ylm thyl]- oxazolidine-, 4-dion ; 5-[4-[2-[N-methyl-N-(2-pyridyl)amino] ethoxy] benzyl]thiazolidine-2,4-dione (BRL 49653); and 5-[4-[2-[N- (benzoxazol -2-yl)-N-methylamino] ethoxy]benzyl]oxazolidine-2,4-dione.

7. (Original) The method of claim 1, wherein the PPAR gamma ligand is selected from the group consisting of PGA_1, PGA_2, PGB_1, PGB_2, PGD_1, PGD_2, PDJ_2, 15-deoxy-12,14-delta-PGJ_2, and 12-delta-PGJ_2.

8. (Original) The method of claim 1, wherein the PPAR gamma ligand is a fatty acid containing about 10 to about 26 carbon atoms and zero to about 6 carbon-carbon double bonds or carbon-carbon triple bonds.

9. (Original) The method of claim 1, wherein the patient has a disease or disorder characterized by undesirable excessive neovascularization.

10. (Original) The method of claim 9, wherein the disease or disorder is selected from the group consisting of a neoplasm, rheumatoid arthritis, psoriasis, atherosclerosis, diabetic and other retinopathy, endometriosis, retrolental fibroplasia, age-related macular degeneration, neovascular glaucoma, thyroid hyperplasia, tissue transplantation, lung inflammation, obesity, and chronic inflammation.

11. (Cancelled)

12. (Previously Amended) A method of inhibiting angiogenesis in a patient, comprising:

(a) identifying a patient with a disease or disorder susceptible to angiogenesis inhibition selected from the group consisting of a neoplasm, rheumatoid arthritis, psoriasis, atherosclerosis, thyroid hyperplasia, endometriosis, lung inflammation, obesity, and chronic inflammation; and

(b) administering an angiogenesis inhibiting amount of a PPAR gamma ligand, wherein angiogenesis is inhibited in the patient.

13. (Cancelled)

14. (Amended) The method of claim ~~13~~12, wherein the ~~mammal~~ patient is a human.

15. (Original) The method of claim 12, further comprising administering a therapeutically effective amount of an RXR receptor ligand.

16. (Original) The method of claim 12, wherein the PPAR gamma ligand is selected from the group consisting of (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy] phenyl]methyl]-2,4-thiazolidinedione: (troglitazone); 5-[4-[2-(5-ethylpyridin-2-yl) ethoxyl]benzyl]thiadiazolidine-2,4-dione:(pioglitazone); 5-[4-[(1-methylcyclohexyl) methoxy]benzyl]thiadiazolidine-2,4-dione: (ciglitazone); 4-(2-naphthylmethyl)- 1,2,3,5- oxathiadiazole-2-oxide; 5-[4-[2-[N-(benzoxazol-2-yl)-N-methylamino]ethoxy]benzyl]-5-methylthiazolidine-2,4-dione; 5-[4-[2-[2,4-dioxo-5-phenylthiazolidin-3-yl) ethoxy] benzyl]thiazolidine-2,4-dione; 5-[4-[2-[N-methyl-N-(phenoxycarbonyl)amino] ethoxy] benzyl]thiazolidine-2,4-dione; 5-[4-[2-phenoxyethoxy) benzyl]thiazolidine-2,4-dione; 5-[4-[2-(4-chlorophenyl) ethylsulfonyl] benzyl]thiazolidine-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl) propionyl]benzyl]thiazolidine-2,4-dione; 5-[[4-(3-hydroxy-1-methylcyclohexyl) methoxy]benzyl]thiadiazolidine-2,4-dione; 5-[4-[2-(5-methyl-2-phenyloxazol-4-yl) ethoxyl]benzyl]thiadiazolidione-2,4-dione; 5-[(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl]thiadiazoline-2,4-dione: (englitazone); 5-[[2-(2-naphthylmethyl) benzoxazol]-5-ylmethyl] thiadiazoline -2,4-dione; 5-[4-[2-(3-phenylureido)ethoxyl] benzyl]thiadiazoline-2,4-dione; 5-[4-[2- [N-(benzoxazol-2-yl)-N- methylamino] ethoxy]benzyl]]thiadiazoline-2,4-dione; 5-[4-[3-(5-methyl-2-phenyloxazol-4-yl) propionyl] benzyl]thiadiazoline-2,4-dione; 5-[2-(5-methyl-2-phenyloxazol-4-ylmethyl) benzofuran- 5-ylmethyl]- oxazolidine-, 4-dione; 5-[4-[2-[N-methyl-N-(2-pyridyl)amino] ethoxy] benzyl]thiazolidine-2,4-dione (BRL 49653); and 5-[4-[2-[N- (benzoxazol -2-yl)-N-methylamino] ethoxy]benzyl]-oxazolidine-2,4-dione.

17. (Original) The method of claim 12, wherein the PPAR gamma ligand is selected from the group consisting of PGA_1, PGA_2, PGB_1, PGB_2, PGD_1, PGD_2, PDJ_2, 15-deoxy-12, 14-delta-PGJ_2, and 1 2-delta-PGJ_2.

18. (Original) The method of claim 12, wherein the PPAR gamma ligand is a fatty acid containing about 10 to about 26 carbon atoms and zero to about 6 carbon-carbon double bonds or carbon-carbon triple bonds.

19-29. (Cancelled)

30. (New) A method of inhibiting angiogenesis comprising:

(a) identifying a patient having a solid malignant tumor; and

(b) administering to the patient a therapeutically effective amount of a PPAR gamma ligand, wherein angiogenesis is inhibited in the patient.

31. (New) A method of inhibiting angiogenesis in a patient, comprising:

(a) identifying a patient with a solid malignant tumor; and

(b) administering an angiogenesis inhibiting amount of a PPAR gamma ligand, wherein angiogenesis is inhibited in the patient.

SUPPORT FOR AMENDMENT

Claim 14 has be n amended to prop rly d pend from claim 12. Claim 30 is supported by claims 1 and 11. Claim 31 is supported by claims 11 and 12. No new matter has been added. Upon entry of this amendment Claims 1-10, 12, and 14-18, 30 and 31 are present and active in the application.

REQUEST FOR RECONSIDERATION

Applicants would like to thank Examiner Qazi for th helpful and courteous discussion held with Applicants' representative on June 24, 2003. During this discussion Applicants' representative noted that the inhibition of angiogenesis is a treatment appropriate for disorders beyond certain cancers, and furthermore is not appropriate for many forms of cancer. It was also noted during the discussion that Urban, et al. only describes that troglitazone inhibits steroidogenesis and applies this compound only to cell lines; there is no indication that this compound has any effect on angiogenesis. Finally, it was also noted that the present claims specify inhibiting angiogenesis. As suggested during the discussion, claims that specify solid malignant tumors have been added (claims 30 and 31).

Angiogenesis is the growth and formation of blood vessels. A variety of diseases and disorders, such as rheumatoid arthritis, psoriasis, atherosclerosis, lung inflammation, obesity, as well as cancer tumor growth and metastasis, can be treated with an angiogenesis inhibitor. The present invention makes use of the discovery that a PPAR gamma ligand is an effective angiogenesis inhibitor.

The rejection of the claims under 375 U.S.C. §103 over Urban, et al. and Cushman, et al., is respectfully traversed. The applied references are silent about troglitazone or a PPAR gamma ligand having any effect on angiogenesis, while the claimed invention is a method of inhibiting angiogenesis.

Urban, et al. describe troglitazone and related compounds for the treatment of climacteric symptoms. Described is that troglitazone and related thiazolidinedione compounds inhibit steroidogenesis in granulosa cells, and that troglitazone can kill rapidly growing cancerous cells expressing the orphan nuclear receptor PPAR gamma, while not affecting the viability of normal cells (column 2, lines 65 - column 3, line 5). The examples describe treating cell lines with troglitazone; no actual tumors or patients having cancer are treated. Examples 7 and 8 are prophetic, and were not actually carried out. There is no description or suggestion of the inhibition of angiogenesis.

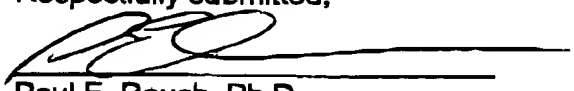
Cushman, et al. describe that angiogenesis is the formation of new blood vessels; there is no suggestion that troglitazone or PPAR gamma ligand may inhibit angiog nesis.

As now claimed, the present invention specifies inhibiting angiogenesis. Urban, et al. fail to describe or suggest inhibiting angiogenesis. Cushman, et al. have only been cited for the definition of angiogenesis. Accordingly, Applicants submit that there is no description or suggestion in the applied references to inhibit angiogenesis with troglitazone or PPAR gamma ligand. Applicants submit that the claimed invention is not obvious over the applied references. Withdrawal of this ground of rejection is respectfully requested.

Applicants respectfully request that all the information disclosure statements be considered. All references cited in the Form 1449 submitted on November 15, 2002 (with the response) were previously cited in the parent application. Accordingly, applicants are not required to submit copies of the references cited (37 C.F.R. § 1.98 (d) (1) and (2)). Furthermore, the information disclosure statement filed by facsimile on November 20, 2002, was filed with a copy of the single reference cited. Copies of both Forms 1449 are included herewith, along with the reference cited in the later Form, as a courtesy to the Examiner. Also included is a copy of the facsimile reported indicating that 9 pages (corresponding to the information disclosure statement, facsimile cover sheet, and the reference cited) were sent on November 20, 2002. Applicants are also in the process of gathering all the references cited in both Forms 1449, and will provide them to the Examiner shortly, as a courtesy.

Applicants submit the application is now in condition for allowance. Early notice of such action is earnestly solicited.

Respectfully submitted,



Paul E. Rauch, Ph.D.
Registration No. 38,591
Attorney for Applicants

SONNENSCHEIN NATH & ROSENTHAL, LLP
P. O. BOX 061080
WACKER DRIVE STATION, SEARS TOWER
CHICAGO, IL 60606
(312) 876-8000

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCL SURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

REFERENCE DESIGNATION		U.S. PATENT DOCUMENTS				
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
	A1	4,287,200	01-09-81	Kawamatsu, et al.		
	A2	4,340,605	20-07-82	Kawamatsu, et al.		
	A3	4,438,141	20-03-84	Kawamatsu, et al.		
	A4	4,444,779	24-04-84	Kawamatsu, et al.		
	A5	4,461,902	24-07-84	Kawamatsu, et al.		
	A6	4,572,912	25-02-86	Yoshioka, et al.		
	A7	4,687,777	18-08-87	Meguro, et al.		17-01-86
	A8	4,703,052	27-10-87	Eggler, et al.		
	A9	4,725,610	16-02-88	Meguro, et al.		
	A10	4,810,804	07-03-89	Chandraratna, R.		
	A11	4,873,255	10-10-89	Yoshioka, et al.		
	A12	4,897,393	30-01-90	Iijima, et al.		
	A13	4,897,405	30-01-90	Alessi, et al.		
	A14	4,918,091	17-04-90	Cantello, et al.		
	A15	4,948,900	14-08-90	Iijima, et al.		
	A16	5,002,953	26-03-91	Hindley, R.		
	A17	5,061,717	29-10-91	Clark, et al.		
	A18	5,120,754	09-06-92	Clark, et al.		
	A19	5,132,317	21-07-92	Cantello, et al.		
	A20	5,194,443	16-03-93	Hindley, R.		
	A21	5,223,522	29-06-93	Clark, et al.		
	A22	5,232,925	03-08-93	Hindley, R.		
	A23	5,260,445	09-11-93	Hindley, R.		
	A24	5,399,586	21-03-95	Davies, et al.		
	A25	5,457,109	10-10-95	Antonucci, et al.		23-08-94
	A26	5,466,861	14-11-95	Dawson, et al.		
	A27	5,478,852	26-12-95	Olefsky, et al.		23-08-94
	A28	5,599,826	04-02-97	Mertens, et al.		19-05-94
	A29	5,646,169	08-07-97	Hindley, et al.		01-06-95
	A30	5,686,596	11-11-97	Mukherjee		
	A31	5,700,682	23-12-97	Mak, et al.		
	A32	5,700,820	23-12-97	Vyas, et al.		19-06-96
	A33	5,710,004	20-01-98	Evans, et al.		

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Nov. 98

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

REFERENCE DESIGNATION		U.S. PATENT DOCUMENTS				
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILIN DATE
	A34	5,714,595	03-02-98	Mak, et al.		
	A35	5,770,378	23-06-98	Hwang, et al.		
	A36	5,770,382	23-06-98	Hwang, et al.		
	A37	5,770,383	23-06-98	Hwang, et al.		
	A38	5,780,676	14-07-98	Boehm, et al.		
	A39	5,811,439	22-09-98	Ogawa, et al.		18-12-96
	A40	5,814,647	29-09-98	Urban, et al.		04-03-97
	A41	5,824,685	20-10-98	Campochiaro, et al.		
	A42	5,902,726	11-05-99	Kliewer, et al.		
	A43	5,925,657	20-07-99	Seed, et al.		
	A44	6,034,110	07-03-00	Nagpal, et al.		

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES	NO
	B1	EPO 953,355	03-11-99	Europe			
	B2	JP 4-69383	04-03-92	Japan			
	B3	JP 62-234085	14-10-87	Japan			
	B4	WO 00/00194	06-01-00	WIPO			
	B5	WO 89/08651	21-09-89	WIPO			
	B6	WO 91/07107	30-05-91	WIPO			
	B7	WO 92/02520	20-02-92	WIPO			
	B8	WO 94/01433	20-01-94	WIPO			
	B9	WO 95/35108	28-12-95	WIPO			
	B10	WO 97/10819	27-03-97	WIPO			
	B11	WO 97/45141	04-12-97	WIPO			
	B12	WO 97/46238	11-12-97	WIPO			
	B13	WO 98/25598	18-06-98	WIPO	31/00	X	
	B14	WO 98/29113	09-07-98	WIPO			
	B15	WO 98/39006	11-09-98	WIPO	31/495	X	
	B16	WO 98/57631	23-12-98	WIPO			
	B17	WO 99/34783	15-07-99	WIPO			
	B18	WO 99/48529	30-09-99	WIPO			

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C1	Bishop-Bailey et al., "Endothelial Cell Apoptosis Induced by the Peroxisome Proliferator-activated Receptor (PPAR) Ligand 15-Deoxy-\104\sup12,\nor\sup14]nor-prostaglindin J\sub2\nor" Journal of Biological Chemistry 274(24):17042-17048(06 11, 1999)
	C2	Brown et al., "Association between expression of activated 72-kilodalton gelatinase and tumor spread in non-small-cell lung carcinoma" Journal of the National Cancer Institute 85(7): 574-578 (Apr 7, 1993)
	C3	Danehower et al., "Troglitazone inhibits proliferation of microvascular endothelial cells; implications for diabetic retinopathy" Diabetologia (Abstract No. 1581 presented at the 16th International Diabetes Federation Congress held in Helsinki, Finland on July 20-25, 1997) 40(suppl. 1):A402 (1997)
	C4	Davis and Camarillo, "An \1412\1421 Integrin-dependent pinocytic mechanism involving intracellular vacuole formation and coalescence regulates capillary lumen and tube formation in three-dimensional collagen matrix" Experimental Cell Research 224(1):39-51 (Apr 10, 1996)
	C5	Elstner et al., "Ligands for peroxisome proliferator-activated receptor\147 and retinoic acid receptor inhibit growth and induce apoptosis of human breast cancer cells in vitro and in BNX mice" Proc. Natl. Acad. Sc. USA 95(15):8806-8811 (Jul 21, 1998)
	C6	Ferrara and David-Smyth, "The biology of vascular endothelial growth factor" Endocrine Reviews 18(1):4-25 (1997)
	C7	Fisher et al., "Interstitial collagenase is required for angiogenesis in vitro" Developmental Biology 162(2):499-510 (Apr 1994)
	C8	Fong et al., "Role of the Fit-1 receptor tyrosine kinase in regulating the assembly of vascular endothelium" Nature 376:66-70 (1995)
	C9	Forman et al., "15-Deoxy-\104\sup12\nor.\sup14\nor-prostaglandin J\sub2\nor is a ligand for the adipocyte determination factor PPAR\147" Cell 83:803-812 (1995)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09600080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C10	Forman et al., "Hypolipidemic drugs, polyunsaturated fatty acids, and eicosanoids are ligands for peroxisome proliferator-activated receptors \141 and \144" Proc. Natl. Acad. Sci. USA 94(9):4312-4317 (Apr 29, 1997)
	C11	Gralinski et al., "Effects of Troglitazone and Pioglitazone on Cytokine-Mediated Endothelial Cell Proliferation in Vitro""Journal of Cardiovascular Pharmacology, Philadelphia:Lippincott-Raven Publishers Vol. 31:909-913 (1998)
	C12	Haas et al., "Three-dimensional type I collagen lattices induce coordinate expression of matrix metalloproteinases MT1-MMP and MMP-2 in microvascular endothelial cells" Journal of Biological Chemistry 273(6):3604-3610 (Feb 6, 1998)
	C13	Hanemaaljer et al., "Regulation of matrix metalloproteinase expression in human vein and microvascular endothelial cells. Effects of tumour necrosis factor\141, interleukin 1 and phorbol ester" Biochemical Journal 296(Pt 3):803-809 (Dec 15, 1993)
	C14	Healy et al., "Angiogenesis: a new theory for endometriosis" Human Reproduction Update 4(5):736-740 (Sep-Oct 1998)
	C15	Hiraoka et al., "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins" Cell 95(3):365-377 (Oct 30, 1998)
	C16	Ilan et al., "Distinct signal transduction pathways are utilized during the tube formation and survival phases of in vitro angiogenesis" Journal of Cell Science 111(Pt 24):3621-3631 (Dec 18, 1998)
	C17	Inoue et al., "Expression of peroxisome proliferator-activated receptor\141 (PPAR\141) in primary cultures of human vascular endothelial cells" Biochemical & Biophysical Research Communications 246(2):370-374 (May 19, 1998)
	C18	Issemann and Green, "Activation of a member of the steroid hormone receptor superfamily by peroxisome proliferators" Nature 347(6294):645-650 (Oct 18, 1990)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C19	Itoh et al., "Unaltered secretion of\142-amyloid precursor protein in gelatinase A (matrix metalloproteinase 2)-deficient mice" Journal of Biological Chemistry 272(36):22389-22392 (Sep 5, 1997)
	C20	Jiang et al., "PPAR-\147 agonists inhibit production of monocyte inflammatory cytokines" Nature 391(6662):82-86 (Jan 1, 1998)
	C21	Johnsen et al., "Cancer invasion and tissue remodeling: common themes in proteolytic matrix degradation" Current Opinion in Cell Biology 10(5):667-671 (Oct 1998)
	C22	Kliewer, S.A., "A prostaglandin J\sub2\nor metabolite binds peroxisome proliferator-activated receptor \147 and promotes adipocyte differentiation"'Cell 83:813-819 (1995)
	C23	Kubota et al., "Ligand for peroxisome proliferator-activated receptor\147 (troglitazone) has potent antitumor effect against human prostate caner both in vitro and in vivo" Cancer Research 58(15):3344-3352 (Aug 1, 1998)
	C24	Lamoreaux et al., "Vascular endothelial growth factor increases release of gelatinase A and decreases release of tissue inhibitor of metalloproteinases by microvascular endothelial cells in vitro" Microvascular Research 55(1):29-42 (Jan 1998)
	C25	Mackay et al., "Effect of phorbol ester and cytokines on matrix metalloproteinase and tissue inhibitor of metalloproteinase expression in tumor and normal cell lines" Invasion & Metastasis 12(3-4):168-184 (1992)
	C26	Marx et al., "Macrophages in human atheroma contain PPAR\147.: Differentiation-dependent peroxisomal proliferator-activated receptor \147 (PPAR\147) expression and reduction of MMP-9 activity through PPAR\147 activation in mononuclear phagocytes in vitro" American Journal of Pathology 153(1):17-23 (Jul 1998)
	C27	Marx et al., "Peroxisome proliferator-activated receptor gamma activators inhibit gene expression and migration in human vascular smooth muscle cells" Circulation Research 83(11:1097-1103 (Nov 30, 1998)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATI N DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C28	Moses, M., "The regulation of neovascularization of matrix metalloproteinases and their inhibitors" Stem Cells 15(3):180-189 (1997)
	C29	Motojima, K., "Toward the treatment of obesity. Role of PPAR gamma in adipogenesis" Tanpakushitasu Kakusan Koso (Abstract only) 40(13):1936-1941 (1995)
	C30	Mukherjee et al., "Identification, characterization, and tissue distribution of human peroxisome proliferator-activated receptor (PPAR) isoforms PPAR\1472 versus PPAR\1471 and activation with retinoid X receptor agonists and antagonists" Journal of Biological Chemistry 272(12):8071-8076 (Mar 21, 1997)
	C31	Mukherjee et al., "Sensitization of diabetic and obese mice to insulin by retoinoid X receptor agonists" Nature 386(6623):407-410 (Mar 27, 1997)
	C32	Murphy et al., "Tissue inhibitor of metalloproteinases-2 inhibits bFGF-induced human microvascular endothelial cell proliferation" Journal of Cellular Physiology 157(2):351-358 (Nov 1993)
	C33	Palmer and Wolf, "cis-parinaric acid is a ligand for the human peroxisome proliferator activated receptor\147: development of a noval spectrophotometric assay for the discovery of PPAR\147 ligands" FEBS Letters 431(3):476-480 (Jul 24, 1998)
	C34	Pershadsingh et al., "Opthalmic uses of PPAR-gamma . . ." Caplus 132:73666 (01 6, 2000)
	C35	Puyraimond et al., "Examining the relationship between the gelatinolytic balance and the invasive capacity of endothelial cells" Journal of Cell Science 112(Pt 9):1283-1290 (May 1999)
	C36	Qian et al., "Thrombospondin-1 modulates angiogenesis in vitro by up-regulation of matrix metalloproteinase-9 in endothelial cells" Experimental Cell Research 235(2):403-412 (Sep 15, 1997)
	C37	Ricote et al., "The peroxisome proliferator-activated receptor-\147 is a negative regulator of macrophage activation" Nature 391(6662):79-82 (Jan 1, 1998)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INF RMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C38	Sarraf et al., "Differentiation and reversal of malignant changes in colon cancer through PPAR\147" Nature Medicine 4(9):1046-1052 (Sep 1998)
	C39	Schnaper et al., "Type IV collagenase(s) and TIMPs modulate endothelial cell morphogenesis in vitro" Journal of Cellular Physiology 156(2):235-246 (Aug 1993)
	C40	Spiegelman, B., "PPAR-\147: adipogenic regulator and thiazolidinedione receptor" Diabetes 47(4):507-514 (Apr 1998)
	C41	Staels et al., "Activation of human aortic smooth-muscle cells is inhibited by PPAR\141 but notby PPAR\147 activators" Nature 393(6687):790-793 (Jun 25, 1998)
	C42	Stetler-Stevenson, W., "Matrix metalloproteinases in angiogenesis; a moving target for therapeutic intervention" Journal of Clinical Investigation 103(9):1237-1241 (May 1999)
	C43	Vu et al., "MMP-9/gelatinase B is a key regulator of growth plate angiogenesis and apoptosis of hypertrophic chondrocytes" Cell 93(3):411-422 (May 1, 1998)
	C44	Westermarck and Kahari, "Regulation of matrix and metalloproteinase expression in tumor invasion" FASEB Journal 13(8):781-792 (May 1999)
	C45	Xin et al., "Peroxisome proliferator-activated receptor gamma (PPAR\147) ligands are potent inhibitors of angiogenesis" FASEB Journal (Abstract #27.4 presented at the Annual Meeting of the Professional Research Scientists for Experimental Biology held in Wash. D.C. on Apr. 17-21, 1999.) 13(4 Part 1):A39 (1999)
	C46	Xin et al., "Peroxisome proliferator-activated receptor\147 ligands are potent inhibitors of angiogenesis in vitro and in vivo" Journal of Biological Chemistry 274(13):9116-9121 (Mar 26, 1999)
	C47	Yamada et al., "Angiogenic effect of lipid hydroperoxide on bovine aortic endothelial cells" J. Cin. Biochem. Nutr. 25(3):121-130 (1998)

1425192v1

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Feb.-97

FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
LIST F PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	FILING DATE May 25, 2001	GROUP ART UNIT 1625
(use several sheets if necessary)	APPLICANT: Mary E. Gerritsen, et al.	

REFERENCE DESIGNATION U.S. PATENT DOCUMENTS						
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATI N YES	NO

	EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
	C1	Kliewer et al., "Fatty acids and eicosanoids regulate gene expression through direct interactions with peroxisome proliferator-activated receptors alpha and beta" Proc. Natl Acad. Sci. USA 94:4318-4323 (April 1997)

1425199v1

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Rev. Nov. 98